

**Amendments to the Claims**

This listing of claims replaces all prior versions, and listings, of claims in the above-identified application:

**1-43. (Canceled)**

**44. (Previously Presented)** A method for detecting a genetic polymorphism in a target polynucleotide comprising:

providing a mutant polymorphism oligonucleotide probe that is complementary to a region on the target polynucleotide that comprises the genetic polymorphism;

providing a universal oligonucleotide probe capable of binding to the target polynucleotide at a region that is conserved in the analogous wild-type polynucleotide;

wherein one oligonucleotide probe constitutes an upstream oligonucleotide comprising, as its 5' end, a nucleoside comprising a 5' leaving group and the other oligonucleotide probe constitutes a downstream oligonucleotide comprising, as its 3' end, a nucleoside comprising a 3' functional group selected from the group consisting of a 3' phosphorothioate, a 3' phosphoroselenoate and a 3' phosphorotelluroate, such that, when both probes are bound to the target polynucleotide, an end of the universal oligonucleotide probe is not directly adjacent to an end of the mutant polymorphism oligonucleotide probe so as to position the 5' leaving group and the 3' functional group in close proximity to one another;

contacting the target polynucleotide with the universal oligonucleotide probe and the mutant polymorphism oligonucleotide probe to yield an autoligated oligonucleotide product comprising the universal oligonucleotide probe and the mutant polymorphism probe; and

detecting the presence of the autoligated oligonucleotide product.

**45. (Previously Presented)** The method of claim 44 wherein at least one of the mutant polymorphism oligonucleotide probe and the universal oligonucleotide probe further comprises a detectable label.

**46. (Previously Presented)** The method of claim 45 wherein the detectable label is a radiolabel.

**47. (Previously Presented)** The method of claim 44 wherein the genetic polymorphism is selected from the group consisting of a single base mutation, a plurality of single base mutations, a deletion, an insertion, and a genetic rearrangement.

**48. (Previously Presented)** The method of claim 44 wherein the nucleotide position of the genetic polymorphism is not the nucleotide position corresponding to the ligation junction end of the mutant polymorphism probe.

**49. (Canceled)**

**50. (Previously Presented)** A method for detecting a genetic polymorphism in a target polynucleotide comprising:

providing a mutant polymorphism oligonucleotide probe of less than 7 nucleotides in length that is complementary to a region on the target polynucleotide that comprises the genetic polymorphism;

providing a wild-type polymorphism oligonucleotide probe that is complementary to a region on an analogous wild-type polynucleotide that is analogous to the region comprising the genetic polymorphism;

providing a universal oligonucleotide probe capable of binding to the target polynucleotide at a region that is conserved in the analogous wild-type polynucleotide;

wherein either (i) the universal oligonucleotide probe constitutes an upstream oligonucleotide comprising, as its 5' end, a nucleoside comprising a 5' leaving group and both polymorphism oligonucleotide probes constitute downstream oligonucleotides comprising, as their 3' ends, a nucleoside comprising a 3' functional group selected from the group consisting of a 3' phosphorothioate, a 3' phosphoroselenoate and a 3' phosphorotelluroate; or (ii) both polymorphism oligonucleotide probes constitute upstream oligonucleotides comprising, as their 5' ends, a nucleoside comprising a 5' leaving group and the universal oligonucleotide probe constitutes a downstream oligonucleotide comprising, as its 3' end, a nucleoside comprising a 3' functional group selected from the group consisting of a 3' phosphorothioate, a 3' phosphoroselenoate and a 3' phosphorotelluroate, such that, when a universal probe and a polymorphism probe are bound to the target polynucleotide, an end of the universal oligonucleotide probe is substantially adjacent to an end of the polymorphism oligonucleotide probe so as to position the 5' leaving group and the 3' functional group in close proximity to one another;

contacting the target polynucleotide with the universal oligonucleotide probe, the wild-type polymorphism oligonucleotide probe and the mutant polymorphism oligonucleotide probe to yield an autoligated oligonucleotide product comprising the universal oligonucleotide probe and either the mutant polymorphism oligonucleotide probe or the wild-type polymorphism oligonucleotide probe; and

detecting the presence of the autoligated oligonucleotide product.

**51. (Previously Presented)** The method of claim 50 wherein at least one of the mutant polymorphism oligonucleotide probe and the universal oligonucleotide probe further comprises a detectable label.

**52. (Previously Presented)** The method of claim 51 wherein the detectable label is a radiolabel.

53. **(Previously Presented)** The method of claim 50 wherein the genetic polymorphism is selected from the group consisting of a single base mutation, a plurality of single base mutations, a deletion, an insertion, and a genetic rearrangement.

54. **(Previously Presented)** The method of claim 50 wherein the nucleotide position of the genetic polymorphism is not the nucleotide position corresponding to the ligation junction end of the mutant polymorphism probe.

55. **(Canceled)**

56. **(Previously Presented)** A method for detecting a genetic polymorphism in a target RNA comprising:

providing a mutant polymorphism oligonucleotide probe that is complementary to a region on the target RNA that comprises the genetic polymorphism;

providing a universal oligonucleotide probe capable of binding to the target RNA at a region that is conserved in the analogous wild-type RNA;

wherein one oligonucleotide probe constitutes an upstream oligonucleotide comprising, as its 5' end, a nucleoside comprising a 5' leaving group and the other oligonucleotide probe constitutes a downstream oligonucleotide comprising, as its 3' end, a nucleoside comprising a 3' functional group selected from the group consisting of a 3' phosphorothioate, a 3' phosphoroselenoate and a 3' phosphorotelluroate, such that, when both probes are bound to the target RNA, an end of the universal oligonucleotide probe is substantially adjacent to an end of the mutant polymorphism oligonucleotide probe so as to position the 5' leaving group and the 3' functional group in close proximity to one another;

contacting the target RNA with the universal oligonucleotide probe and the mutant polymorphism oligonucleotide probe to yield an autoligated oligonucleotide product comprising the universal oligonucleotide probe and the mutant polymorphism probe; and

detecting the presence of the autoligated oligonucleotide product.

57. **(Previously Presented)** The method of claims 56 wherein at least one of the mutant polymorphism oligonucleotide probe and the universal oligonucleotide probe further comprises a detectable label.

58. **(Previously Presented)** The method of claim 57 wherein the detectable label is a radiolabel.

59. **(Previously Presented)** The method of claim 56 wherein the genetic polymorphism is selected from the group consisting of a single base mutation, a plurality of single base mutations, a deletion, an insertion, and a genetic rearrangement.

60. **(Previously Presented)** The method of claim 56 wherein the nucleotide position is not the nucleotide position corresponding to the ligation junction end of the mutant polymorphism probe.

61-63. **(Canceled)**

64. **(New)** A method for detecting a genetic polymorphism in a target polynucleotide comprising:

providing a mutant polymorphism oligonucleotide probe that is complementary to a region on the target polynucleotide that comprises the genetic polymorphism;

providing a universal oligonucleotide probe capable of binding to the target polynucleotide at a region that is conserved in the analogous wild-type polynucleotide;

wherein one oligonucleotide probe constitutes an upstream oligonucleotide comprising, as its 5' end, a nucleoside comprising a 5' leaving group and the other

oligonucleotide probe constitutes a downstream oligonucleotide comprising, as its 3' end, a nucleoside comprising a 3' functional group selected from the group consisting of a 3' phosphorothioate, a 3' phosphoroselenoate and a 3' phosphorotelluroate, such that, when both probes are bound to the target polynucleotide, either (a) there is a gap of 1 or 2 bases between an end of the universal oligonucleotide probe and an end of the mutant polymorphism oligonucleotide probe, or (b) there is a 1 or 2 nucleotide overlap between an end of the universal oligonucleotide probe and an end of the mutant polymorphism oligonucleotide probe, so as to position the 5' leaving group and the 3' functional group in close proximity to one another; contacting the target polynucleotide with the universal oligonucleotide probe and the mutant polymorphism oligonucleotide probe to yield an autoligated oligonucleotide product comprising the universal oligonucleotide probe and the mutant polymorphism probe; and detecting the presence of the autoligated oligonucleotide product.

65. **(New)** A method for detecting a genetic polymorphism in a target polynucleotide comprising:

providing a mutant polymorphism oligonucleotide probe that is complementary to a region on the target polynucleotide that comprises the genetic polymorphism;

providing a universal oligonucleotide probe capable of binding to the target polynucleotide at a region that is conserved in the analogous wild-type polynucleotide;

wherein one oligonucleotide probe constitutes an upstream oligonucleotide comprising a sequence of nucleotides, wherein the nucleotide at its 5' end comprises a nucleoside comprising a 5' leaving group, and the other oligonucleotide probe constitutes a downstream oligonucleotide comprising a sequence of nucleotides, wherein the nucleotide at its 3' end comprises a nucleoside comprising a 3' functional group selected from the group consisting of a 3' phosphorothioate, a 3' phosphoroselenoate and a 3' phosphorotelluroate, such that, when both probes are bound to the target polynucleotide, an end of the universal oligonucleotide probe is

not directly adjacent to an end of the mutant polymorphism oligonucleotide probe so as to position the 5' leaving group and the 3' functional group in close proximity to one another;

contacting the target polynucleotide with the universal oligonucleotide probe and the mutant polymorphism oligonucleotide probe to yield an autoligated oligonucleotide product comprising the universal oligonucleotide probe and the mutant polymorphism probe; and detecting the presence of the autoligated oligonucleotide product.

66. (New) A method for detecting a genetic polymorphism in a target polynucleotide comprising:

providing a mutant polymorphism oligonucleotide probe that is complementary to a region on the target polynucleotide that comprises the genetic polymorphism;

providing a universal oligonucleotide probe capable of binding to the target polynucleotide at a region that is conserved in the analogous wild-type polynucleotide;

wherein one oligonucleotide probe constitutes an upstream oligonucleotide comprising a sequence of nucleotides, wherein the nucleotide at its 5' end comprises a nucleoside comprising a 5' leaving group, and the other oligonucleotide probe constitutes a downstream oligonucleotide comprising a sequence of nucleotides, wherein the nucleotide at its 3' end comprises a nucleoside comprising a 3' functional group selected from the group consisting of a 3' phosphorothioate, a 3' phosphoroselenoate and a 3' phosphorotelluroate, such that, when both probes are bound to the target polynucleotide, either (a) there is a gap of 1 or 2 bases between an end of the universal oligonucleotide probe and an end of the mutant polymorphism oligonucleotide probe, or (b) there is a 1 or 2 nucleotide overlap between an end of the universal oligonucleotide probe and an end of the mutant polymorphism oligonucleotide probe, so as to position the 5' leaving group and the 3' functional group in close proximity to one another;

contacting the target polynucleotide with the universal oligonucleotide probe and the mutant polymorphism oligonucleotide probe to yield an autoligated oligonucleotide product comprising the universal oligonucleotide probe and the mutant polymorphism probe; and

detecting the presence of the autoligated oligonucleotide product.

67. **(New)** A method for detecting a genetic polymorphism in a target polynucleotide comprising:

- providing a mutant polymorphism oligonucleotide probe of less than 7 nucleotides in length that is complementary to a region on the target polynucleotide that comprises the genetic polymorphism;

- providing a wild-type polymorphism oligonucleotide probe that is complementary to a region on an analogous wild-type polynucleotide that is analogous to the region comprising the genetic polymorphism;

- providing a universal oligonucleotide probe capable of binding to the target polynucleotide at a region that is conserved in the analogous wild-type polynucleotide;

- wherein either (i) the universal oligonucleotide probe constitutes an upstream oligonucleotide comprising, as its 5' end, a nucleoside comprising a 5' leaving group, and both polymorphism oligonucleotide probes constitute downstream oligonucleotides comprising, as their 3' ends, a nucleoside comprising a 3' functional group selected from the group consisting of a 3' phosphorothioate, a 3' phosphoroselenoate and a 3' phosphorotelluroate; or (ii) both polymorphism oligonucleotide probes constitute upstream oligonucleotides comprising, as their 5' ends, a nucleoside comprising a 5' leaving group, and the universal oligonucleotide probe constitutes a downstream oligonucleotide comprising, as its 3' end, a nucleoside comprising a 3' functional group selected from the group consisting of a 3' phosphorothioate, a 3' phosphoroselenoate and a 3' phosphorotelluroate, such that, when a universal probe and a polymorphism probe are bound to the target polynucleotide, either (a) an end of the universal oligonucleotide probe is directly adjacent to an end of the polymorphism oligonucleotide probe, (b) there is a gap of 1 or 2 bases between an end of the universal oligonucleotide probe and an end of the polymorphism oligonucleotide probe, or (c) there is a 1 or 2 nucleotide overlap between an end of the universal oligonucleotide probe and an end of the polymorphism



oligonucleotide probe, so as to position the 5' leaving group and the 3' functional group in close proximity to one another;

contacting the target polynucleotide with the universal oligonucleotide probe, the wild-type polymorphism oligonucleotide probe and the mutant polymorphism oligonucleotide probe to yield an autoligated oligonucleotide product comprising the universal oligonucleotide probe and either the mutant polymorphism oligonucleotide probe or the wild-type polymorphism oligonucleotide probe; and

detecting the presence of the autoligated oligonucleotide product.

68. (New) A method for detecting a genetic polymorphism in a target polynucleotide comprising:

providing a mutant polymorphism oligonucleotide probe of less than 7 nucleotides in length that is complementary to a region on the target polynucleotide that comprises the genetic polymorphism;

providing a wild-type polymorphism oligonucleotide probe that is complementary to a region on an analogous wild-type polynucleotide that is analogous to the region comprising the genetic polymorphism;

providing a universal oligonucleotide probe capable of binding to the target polynucleotide at a region that is conserved in the analogous wild-type polynucleotide;

wherein either (i) the universal oligonucleotide probe constitutes an upstream oligonucleotide comprising a sequence of nucleotides, wherein the nucleotide at its 5' end comprises a nucleoside comprising a 5' leaving group, and both polymorphism oligonucleotide probes constitute downstream oligonucleotides comprising sequences of nucleotides, wherein the nucleotide at their 3' ends comprises a nucleoside comprising a 3' functional group selected from the group consisting of a 3' phosphorothioate, a 3' phosphoroselenoate and a 3' phosphorotelluroate; or (ii) both polymorphism oligonucleotide probes constitute upstream oligonucleotides comprising sequences of nucleotides, wherein the nucleotide at their 5' ends

comprises a nucleoside comprising a 5' leaving group, and the universal oligonucleotide probe constitutes a downstream oligonucleotide comprising a sequence of nucleotides, wherein the nucleotide at its 3' end comprises a nucleoside comprising a 3' functional group selected from the group consisting of a 3' phosphorothioate, a 3' phosphoroselenoate and a 3' phosphorotelluroate, such that, when a universal probe and a polymorphism probe are bound to the target polynucleotide, an end of the universal oligonucleotide probe is substantially adjacent to an end of the polymorphism oligonucleotide probe so as to position the 5' leaving group and the 3' functional group in close proximity to one another;

contacting the target polynucleotide with the universal oligonucleotide probe, the wild-type polymorphism oligonucleotide probe and the mutant polymorphism oligonucleotide probe to yield an autoligated oligonucleotide product comprising the universal oligonucleotide probe and either the mutant polymorphism oligonucleotide probe or the wild-type polymorphism oligonucleotide probe; and

detecting the presence of the autoligated oligonucleotide product.

69. **(New)** A method for detecting a genetic polymorphism in a target polynucleotide comprising:

providing a mutant polymorphism oligonucleotide probe of less than 7 nucleotides in length that is complementary to a region on the target polynucleotide that comprises the genetic polymorphism;

providing a wild-type polymorphism oligonucleotide probe that is complementary to a region on an analogous wild-type polynucleotide that is analogous to the region comprising the genetic polymorphism;

providing a universal oligonucleotide probe capable of binding to the target polynucleotide at a region that is conserved in the analogous wild-type polynucleotide;

wherein either (i) the universal oligonucleotide probe constitutes an upstream oligonucleotide comprising a sequence of nucleotides, wherein the nucleotide at its 5' end

comprises a nucleoside comprising a 5' leaving group, and both polymorphism oligonucleotide probes constitute downstream oligonucleotides comprising sequences of nucleotides, wherein the nucleotide at their 3' ends comprises a nucleoside comprising a 3' functional group selected from the group consisting of a 3' phosphorothioate, a 3' phosphoroselenoate and a 3' phosphorotelluroate; or (ii) both polymorphism oligonucleotide probes constitute upstream oligonucleotides comprising sequences of nucleotides, wherein the nucleotide at their 5' ends comprises a nucleoside comprising a 5' leaving group, and the universal oligonucleotide probe constitutes a downstream oligonucleotide comprising a sequence of nucleotides, wherein the nucleotide at its 3' end comprises a nucleoside comprising a 3' functional group selected from the group consisting of a 3' phosphorothioate, a 3' phosphoroselenoate and a 3' phosphorotelluroate, such that, when a universal probe and a polymorphism probe are bound to the target polynucleotide, either (a) an end of the universal oligonucleotide probe is directly adjacent to an end of the polymorphism oligonucleotide probe, (b) there is a gap of 1 or 2 bases between an end of the universal oligonucleotide probe and an end of the polymorphism oligonucleotide probe, or (c) there is a 1 or 2 nucleotide overlap between an end of the universal oligonucleotide probe and an end of the polymorphism oligonucleotide probe, so as to position the 5' leaving group and the 3' functional group in close proximity to one another;

contacting the target polynucleotide with the universal oligonucleotide probe, the wild-type polymorphism oligonucleotide probe and the mutant polymorphism oligonucleotide probe to yield an autoligated oligonucleotide product comprising the universal oligonucleotide probe and either the mutant polymorphism oligonucleotide probe or the wild-type polymorphism oligonucleotide probe; and

detecting the presence of the autoligated oligonucleotide product.

**70. (New)** A method for detecting a genetic polymorphism in a target RNA comprising:

providing a mutant polymorphism oligonucleotide probe that is complementary to a region on the target RNA that comprises the genetic polymorphism;

providing a universal oligonucleotide probe capable of binding to the target RNA at a region that is conserved in the analogous wild-type RNA;

wherein one oligonucleotide probe constitutes an upstream oligonucleotide comprising, as its 5' end, a nucleoside comprising a 5' leaving group and the other oligonucleotide probe constitutes a downstream oligonucleotide comprising, as its 3' end, a nucleoside comprising a 3' functional group selected from the group consisting of a 3' phosphorothioate, a 3' phosphoroselenoate and a 3' phosphorotelluroate, such that, when both probes are bound to the target RNA, either (a) an end of the universal oligonucleotide probe is adjacent to an end of the mutant polymorphism oligonucleotide probe, (b) there is a gap of 1 or 2 bases between an end of the universal oligonucleotide probe and an end of the mutant polymorphism oligonucleotide probe, or (c) there is a 1 or 2 nucleotide overlap between an end of the universal oligonucleotide probe and an end of the mutant polymorphism oligonucleotide probe, so as to position the 5' leaving group and the 3' functional group in close proximity to one another;

contacting the target RNA with the universal oligonucleotide probe and the mutant polymorphism oligonucleotide probe to yield an autoligated oligonucleotide product comprising the universal oligonucleotide probe and the mutant polymorphism probe; and

detecting the presence of the autoligated oligonucleotide product.

**71. (New)** A method for detecting a genetic polymorphism in a target RNA comprising:

providing a mutant polymorphism oligonucleotide probe that is complementary to a region on the target RNA that comprises the genetic polymorphism;

providing a universal oligonucleotide probe capable of binding to the target RNA at a region that is conserved in the analogous wild-type RNA;

wherein one oligonucleotide probe constitutes an upstream oligonucleotide comprising a sequence of nucleotides, wherein the nucleotide at its 5' end comprises a nucleoside comprising a 5' leaving group, and the other oligonucleotide probe constitutes a downstream

oligonucleotide comprising a sequence of nucleotides, wherein the nucleotide as its 3' end comprises a nucleoside comprising a 3' functional group selected from the group consisting of a 3' phosphorothioate, a 3' phosphoroselenoate and a 3' phosphorotelluroate, such that, when both probes are bound to the target RNA, an end of the universal oligonucleotide probe is substantially adjacent to an end of the mutant polymorphism oligonucleotide probe so as to position the 5' leaving group and the 3' functional group in close proximity to one another;

contacting the target RNA with the universal oligonucleotide probe and the mutant polymorphism oligonucleotide probe to yield an autoligated oligonucleotide product comprising the universal oligonucleotide probe and the mutant polymorphism probe; and

detecting the presence of the autoligated oligonucleotide product.

**72. (New)** A method for detecting a genetic polymorphism in a target RNA comprising:

providing a mutant polymorphism oligonucleotide probe that is complementary to a region on the target RNA that comprises the genetic polymorphism;

providing a universal oligonucleotide probe capable of binding to the target RNA at a region that is conserved in the analogous wild-type RNA;

wherein one oligonucleotide probe constitutes an upstream oligonucleotide comprising a sequence of nucleotides, wherein the nucleotide at its 5' end comprises a nucleoside comprising a 5' leaving group, and the other oligonucleotide probe constitutes a downstream oligonucleotide comprising a sequence of nucleotides, wherein the nucleotide at its 3' end comprises a nucleoside comprising a 3' functional group selected from the group consisting of a 3' phosphorothioate, a 3' phosphoroselenoate and a 3' phosphorotelluroate, such that, when both probes are bound to the target RNA, either (a) an end of the universal oligonucleotide probe is adjacent to an end of the mutant polymorphism oligonucleotide probe, (b) there is a gap of 1 or 2 bases between an end of the universal oligonucleotide probe and an end of the mutant polymorphism oligonucleotide probe, or (c) there is a 1 or 2 nucleotide overlap between an end of the universal oligonucleotide probe and an end of the mutant polymorphism oligonucleotide

**Amendment and Response**

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DETECTION OF GENETIC POLYMORPHISMS

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probe, so as to position the 5' leaving group and the 3' functional group in close proximity to one another;

contacting the target RNA with the universal oligonucleotide probe and the mutant polymorphism oligonucleotide probe to yield an autoligated oligonucleotide product comprising the universal oligonucleotide probe and the mutant polymorphism probe; and  
detecting the presence of the autoligated oligonucleotide product.